References on Arthritis Research Using ALZET® Osmotic Pumps


ALZET Comments: Antibody A11; compound 59; Saline; IP, SC; Mice; 1004, 2004; 4 weeks, 8 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6J, 25-30g); pumps replaced every 4 weeks; Dose (Antibody: 1.5 ug/day; Compound 59: 5, 25, or 50 mg/kg/day);


ALZET Comments: T140; PBS; SC; Guinea pig; 2006; Dose (180 ug/d); Controls received mp w/ vehicle; animal info (9 month old male Hartley guinea pigs weighing about 600g); pumps replaced every 6 weeks; Therapeutic indication (osteoarthritis);


ALZET Comments: Interleukin-1 receptor antagonist; Saline; IP; Mice; 1007D; 2 weeks; Dose (37.5 ug/hr); Controls received empty mp; animal info (12 week old female C57BL/6 mice);


ALZET Comments: Tofacitinib; PEG 300; CSF/CNS; Mice; 2002; 6 days; animal info (Wild-type CD1); Controls received mp w/vehicle; dose (15 mg/kg/day); cancer; enzyme inhibitor (JAK3);


ALZET Comments: Antibody (hCRACM1-IgG); YM-58483; Saline; Intralipose; SC; Mice; 1004; 28 days; hCRACM1-IgG Dose (1 or 10 mg/kg), YM058483 Dose (1.5mg/kg); YM-58483 was mixed with 10% Intralipose, which is an i.v. lipid emulsion containing 10% soybean oil, 1.2% egg yolk phospholipids, and 2.2% glycerin; Controls received mp w/ vehicle; hCRACM1-IgG is a neutralizing monoclonal antibody targeting human CRACM1; YM-58483 is a small molecular CRAC blocker; Immunology (transplant);


ALZET Comments: Nicotine; PBS; SC; Mice; 2006; 42 days; Dose (15 mg/kg/day); Controls received mp w/ vehicle; animal info (male DBA/1j mice);


ALZET Comments: Prolactin; SC; Rat; 28 days; animal info (Male Sprague-Dawley rats weighing 200–250 g);


ALZET Comments: Morphine hydrochloride; SC; Rat; 2ML1; 5 days; Dose (41–48 mg/kg/day); animal info (8-week-old male Wistar rats weighing 200–240 g); Therapeutic indication (Knee arthritis);


ALZET Comments: Peficitinib; PEG, Acetic acid; IP; Rat; 2ML2; Dose (0.12, 0.24, and 0.48 mg/day per body); Controls received mp w/ vehicle; Resultant plasma level (7.0 ng/mL,18 ng/mL, and 35 ng/mL on day 13, and 7.1 ng/mL, 13 ng/mL, and 30 ng/mL on day 16);
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Bibliography

**ALZET Comments:** AMD3100; PBS; SC; Rat; 2006; 6 weeks; Controls received mp w/ vehicle; animal info (16 weeks old, Sprague-Dawley; 400-500 g); Therapeutic indication (Osteoarthritis, subchondral bone); Dose (22.3 mg/ml).

**ALZET Comments:** AMD3100; PBS; Rat; 2004; 8 weeks; Dose (3 mg/day); Controls received mp w/ vehicle; animal info (8 week old male Sprague-Dawley rats weighing 190-210g); pumps replaced every 4 weeks; Therapeutic indication (osteoarthritis).

Q4897: Gisela Segond von Banchet, et al. Long-Lasting Activation of the Transcription Factor CREB in Sensory Neurons by Interleukin-1b During Antigen-Induced Arthritis in Rats. ARTHRITIS & RHEUMATOLOGY 2016;68(2):532-541
**ALZET Comments:** Anakinra; SC; Rat; 2ML4; 26 days; Controls received mp w/ saline; animal info (female, Lewis, 6-8 weeks old, 160-180g); immunology; delayed delivery for 5 days; Dose (53 mg/kg/day).

**ALZET Comments:** AMD3100; PBS; Mice; 1004; 30 days; Controls received mp w/ vehicle and sham operation; animal info (C57BL/6J mice (30 males, 2 months old)); immunology; (AMD3100 is an immunostimulant); inhibitor of CXCR4; transected the anterior cruciate ligament on the right knee; caused joint instability; Dose (180 ug/day).

Q4613: N. P. Thomas, et al. Attenuation of cartilage pathogenesis in post-traumatic osteoarthritis (PTOA) in mice by blocking the stromal derived factor 1 receptor (CXCR4) with the specific inhibitor, AMD3100. JOURNAL OF ORTHOPAEDIC RESEARCH 2015;33(1071-1078
**ALZET Comments:** AMD3100; SC; Mice; 1004; 2 months; Controls received mp w/ PBS or empty pumps; animal info (male, C57BL6J, 2 months old); pumps replaced every 4 weeks.

Q4279: M. Radwan, et al. Protection against murine osteoarthritis by inhibition of the 26S proteasome and lysine-48 linked ubiquitination. ANNLAS OF THE RHEUMATIC DISEASES 2015;74(1580-1587
**ALZET Comments:** MG132; DMSO; PEG 300; SC; Mice; 1004; 8 weeks; Controls received mp w/ vehicle; animal info (C57BOl6J or mutant-Ub transgenic, 8 weeks old); pumps replaced every 4 weeks; 50% DMSO used; 50% PEG 300; enzyme inhibitor (proteasome, general).

**ALZET Comments:** Calcitonin gene-related peptide (8-37); CSF/CNS (intrathecal); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (female, Lewis, 180-200g); behavioral testing (Von Frey filaments; Plantar test); immunology; peptides.

**ALZET Comments:** Peptide, OP3-4; PBS; DMSO; SC; Mice; 49 days; Controls received mp w/ vehicle; animal info (male, DBA/1J, 7 weeks old); pumps replaced after day 35 or 42; 20% DMSO used; peptides; "a sustained-release carrier for OP3-4 needs to be developed since peptide drugs are unstable and aggregate easily in vivo. The effects of OP3-4 in this study were achieved using infusion pumps" pg 13.

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**ALZET Comments**: AG1478; RS504393; DMSO; water, deionized; SC; Rat; 10 weeks; Controls received mp w/ vehicle; functionality of mp verified by plasma levels and knee articular cartilage; pumps replaced every 4 weeks; %50 of DMSO used; long-term study; enzyme inhibitor (EGFR and CCR2 inhibitors); EGFR inhibitor AG1478, CCR2 inhibitor RS504393; Dose: (AG1478) 21 nmoles/kg/hour; (RS504393) 200 nmoles/kg/hour.

**Q4022**: K. Nishimura, *et al.* Tofacitinib Facilitates the Expansion of Myeloid-Derived Suppressor Cells and Ameliorates Arthritis in SKG Mice. *Arthritis & Rheumatology* 2014;66(S1271-S1272

**ALZET Comments**: Tofacitinib; DMSO; SC; Mice; 5 days; Controls received mp w/ vehicle; animal info (female, SKG mice, arthritis induction); immunology; enzyme inhibitor (JAK3).


**ALZET Comments**: CT99021; DMSO; PEG 400; SC; Mice; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6J, 10 weeks old); 50% PEG 400 used; 50% DMSO used; CT99021 is a GSK-3 inhibitor.


**ALZET Comments**: Interleukin-1 receptor antagonist; Saline; SC; Mice; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6J, 8 weeks old); functionality of mp verified by serum levels; comparison of injection vs mp; stress/adverse reaction: (see pg. 4); post op. care (buprenorphine); "...no significant differences were detected for any of the outcome measures in mice receiving systemic saline via osmotic pump or IP injections." pg 4; pumps removed after 28 days.


**ALZET Comments**: Tofacitinib; DMSO; PEG 300; SC; Mice; 36 days; Controls received mp w/ vehicle; animal info (male, DBA/1, 10-12 weeks old); functionality of mp verified by serum levels at 21 days; 33% DMSO used; dose-response (pg. 168); toxicology; immunology; Tofacitinib is a janus kinase inhibitor; enzyme inhibitor (JAK3).


**ALZET Comments**: Prolactin, ovine; SC; Rat; 6 days; 21 days; Animal info (male, Sprague Dawley, 200-250g); functionality of mp verified by serum levels at 21 days; behavioral testing (hind paw pain); immunology.


**ALZET Comments**: AMD 3100; PBS; SC; Guinea pig; 2006; 12 weeks; Controls received mp w/ PBS; animal info (0.88 kg+0.21 kg); pumps replaced once every 6 weeks; long-term study.

**Q2585**: E. Schurgers, *et al.* Pulmonary inflammation in mice with collagen-induced arthritis is conditioned by complete Freund's adjuvant and regulated by endogenous IFN-γ European Journal of Immunology 2012;42(12):3223-3234

**ALZET Comments**: Etanercept; PBS; Mice; 2004; Control animals received mp w/ vehicle; animal info (IFN gamma R KO, DBA/1).

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Bibliography

ALZET Comments: Cathepsin S; fractalkine; CSF/CNS (intrathecal); Rat; 2001; Animal info (adult, female, Lewis, 180-200 g); peptides.

ALZET Comments: Anakinra; SC; Rat; 1 week; Animal info (male, Lewis, 6-9 wks old); half-life "4-6 hours" pg 78; pharmacokinetic study; pk study.

ALZET Comments: APO866; Propylene glycol; saline; SC; Mice; 1002; 14 days; Controls received mp w/ vehicle; animal info (male, DBA/1, 7-8 wks old); half-life (~8 hours in humans pg 1876); APO866 is a small molecule inhibitor in human fibroblasts in vitro and in murine collagen arthritis; A maximum tolerated dose of APO866 of 0.126 mg/m2/hour in human clinical trials and 0.18 mg/m2/hour in rats has been reported" pg 1868.

ALZET Comments: Anakinra; Saline; sodium citrate; EDTA; tween 80; SCF/CNS (intrathecal); Rat; 2ML1; 7 days; Controls received vehicle; animal info (male, Lewis, 7-9 weeks old; adjuvant-induced arthritis); IL-1B antagonist; 0.5mM EDTA; 0.1% Tween 80.

ALZET Comments: Etanercept; CSF/CNS (intrathecal); Rat; 2ML4; 3, 21 days; Controls received mp w/ vehicle; tolerance; ALZET brain infusion kit used; schematic drawing with ALZET pump and catheter.

Q0005: M. K. Boettger, et al. Spinally applied ketamine or morphine attenuate peripheral inflammation and hyperalgesia in acute and chronic phases of experimental arthritis. BRAIN BEHAVIOR AND IMMUNITY 2010;24(3):474-485
ALZET Comments: Ketamine, Morphine; Saline; CSF/CNS (intrathecal); Rat; 2ML4; 21 days; Controls received mp w/ vehicle; tolerance; ALZET brain infusion kit used; half-life pg 477 (2.5 hrs in CSF (ketamine); 2.1 hrs (morphine)); animal info (Female, Lewis, 6-8 wks old, 160-180 g); dorsal laminectomy; behavioral testing (pain related behavior).

P9905: M. Stolina, et al. RANKL inhibition by osteoprotegerin prevents bone loss without affecting local or systemic inflammation parameters in two rat arthritis models: comparison with anti-TNF-alpha or anti-IL-1 therapies. ARTHRITIS RESEARCH & THERAPY 2009;11(6):U251-U265
ALZET Comments: Anakinra; SC; Rat; Animal info (Lewis, 7 to 8 wks old, AIA, CIA).

ALZET Comments: CP-690550; PEG 300; SC; Rat; mice; 2004; 2ML2; 2 weeks; 28 days; Controls received mp w/ vehicle or no pump; dose-response (fig. 1); enzyme inhibitor (JAK3, janus kinase 3); animal info (male, DBA/J1, male, Lewis); "it was necessary to administer CP-690550 via osmotic pumps due to the poor (PK) properties of this compound in rodents.".

ALZET Comments: Interleukin-10; interleukin-1 receptor antagonist; Saline; DMSO; SC; Mice (SCID); 2004; 40 days; Controls received mp w/ vehicle; functionality of mp verified by plasma levels; good methods (p.125); peptides; animal info (female, SCID, 4-5 wks old); Rheumatoid arthritis; pump and technique schematics p. 125; stability (with an excellent description of methods) was verified for 40 days @ 37C; 50% DMSO used; "... the application of proteins via osmotic pumps is an effective tool to evaluate the effects of cytokines and inhibitors in vitro." p. 128.

ALZET Comments: Anakinra; NaCl; citric acid; EDTA; tween 80; IP; Mice; 1007D; 7 days; Anakinra is an interleukin-1 receptor antagonist; 0.35mM EDTA; 0.07% Tween 80;


ALZET Comments: Estradiol, 2-methoxy-; SC; Rat; 2ML4; 18 days; Controls received mp w/ vehicle; comparison of oral gavage vs. mp; animal info (syngeneic LOU, 8-10 wks old, 100-150 g,). Collagen-induced arthritis; "Delivery of 60 mg/kg by an osmotic pump, however, was similar in efficacy to 300 mg/kg oral gavage. This result suggests that a steady-state level of 2ME2 achieved equivalent arthritic inhibition at a lower total dose." (p. 2124).


ALZET Comments: Osteogenic protein-1; Lactose; Knee (articular cavity); Rabbit; 2004; 6 weeks; Controls received mp w/ vehicle; functionality of mp verified by separate in vivo test; peptides; post op. care ("appropriate"); animal info (New Zealand, White, 1 yr old); also known as BMP-7 or bone morphogenic protein-7; catheter was secured with polyethylene stents; "The efficacy of the (ALZET Pump) was tested in vivo before beginning the study with good results"; "constant infusion of OP-1 may be the most ideal form of delivery"; long-term study; good methods.


ALZET Comments: Nerve growth factor, recomb. human; glial-derived neurotrophic factor, recomb. human; leukemia inhibitory factor, recomb. human; Saline; albumin, rat serum; CSF/CNS (intrathecal); Rat; 2002; 14 days; Controls received mp w/ vehicle; peptides, animal info (male, Wistar, 220-400 g.).


ALZET Comments: TN14003, 4F-benzoyl-; SC; Mice; Mice (SCID); Cancer (breast carcinoma); immunology; peptides; CXCR4 antagonist; review, see p. 21, 23.


ALZET Comments: Peptide, WP9QY; antibody, monoclonal, anti-TNF alpha; PBS; DMSO; SC; Mice; 2001; 19 days; Controls received mp w/ vehicle; dose-response (fig. 1); pumps replaced every 7 days; half-life (p. 1182) "short;" peptides; animal info (male, DBA/1J, 6 weeks old, collagen induced arthritis); 10% DMSO.


ALZET Comments: Infliximab; immunoglobulin G, human; SC; Mice (SCID); 2 weeks; Controls received mp w/ human IgG; immunology; animal info (SCID-HuRaG-pit, 6-7 wks old; TNF-alpha inhibitor.


ALZET Comments: Endostatin; PBS; IP; Mice; 2 weeks; Controls received mp w/ vehicle; animal info (1J, 6 week); "compared with the once daily dosing regimen, the administration of endostatin by an osmotic pump achieved a similar arthritis-inhibiting effect at one-tenth of the dose...the administration method using osmotic pump is useful." pg. 434.
ALZET Comments: Etanercept; Water, sterile; SC; Mice; 2004; 28 days; Controls received mp w/vehicle; animal info (male, DBA/1, wt, IFNγR-KO, 8-12 weeks old).

ALZET Comments: Anakinra; SC; Rat; 4 weeks; Animal info (female, Lewis, 200g.).

ALZET Comments: Estradiol, 17β; PEG; Rat; 2002; 14 days; Animal info (OVX, Sprague-Dawley, 200-225 g, female).

ALZET Comments: Fentanyl; Saline; SC; Rat; 2ML1; 5 days; Controls received mp w/ vehicle; tolerance; animal info (male, Wistar, 250-320 g).

ALZET Comments: AMD 3100; SC; Mice; 2002; 14 days; Controls received mp w/ PBS; immunology; animal info (male, 8-12 weeks).

ALZET Comments: Interleukin-1 receptor antagonist; SC; Mice (transgenic); 2004; 4 weeks;

ALZET Comments: TN14003, 4F-benzoyl-; PBS; SC; Mice; 1007D; 2002; 7,14 days; Controls received mp w/ vehicle; dose-response (Fig.2); immunology; peptides.

ALZET Comments: Muscimol; bicuculline; Saline; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; dose-response; no stress (see pg. 455-6).

R0219: W. B. Van Den Berg. Is there a rationale for combined TNF and IL-1 blocking in arthritis? Clinical and Experimental Rheumatology 2002;20(Suppl. 28):S21-S25
ALZET Comments: Insulin-like growth factor I, receptor antagonist; Mice; "In mice full protection is only achieved with continued dosing in ALZET minipumps." (p. S-24).

ALZET Comments: Transforming Growth Factor-B2, soluble receptor; Polymyxin B; IP; mice; 1007D; 2002; 7,14 or 21 days; Arthritis; controls received empty pumps or mp w/ vehicle; functionality of mp verified by residual aspiration; pumps replaced after 14 days; stability verified by ELISA after infusion (p. 508, 510); soluble TGF-B RII selectively inhibits transforming growth factor-B; peptides; polymyxin B included as endotoxin inhibitor; 2002 pumps used for 7 and 14 day administration, 21-day group received a 1007D pump for final 7 days.

ALZET Comments: Tumor necrosis factor-a; Interleukin-6; Serum, fetal bovine; Culture medium, RPMI 1640; SC; Mice (SCID); 1007D; 7 days; controls received mp w/ vehicle; functionality of mp verified by serum cytokine levels; immunology; peptides; cytokines were recombinant; pump incorrectly called an osmium pump (p. 331); agents administered singly.


ALZET Comments: Placental growth factor; vascular endothelial growth factor; SC; Mice; 2001; 7 days; Angiogenesis.


ALZET Comments: Interleukin-1 receptor antagonist; Saline; sodium citrate; EDTA; Tween 80; SC; Rat; 2ML1; 7 days; Controls received mp w/ BSA "to control for nonspecific anti-angiogenic effects of stress associated with implantation of the osmotic minipump." (p. 2605); implantation of pumps delivering BSA caused no angiogenesis; 0.5mM EDTA; 0.1% Tween 80;.


ALZET Comments: SC; Rabbit; 14 days; Peptides.


ALZET Comments: Naloxone; Naloxone methiodide; Saline; SC; Rat; 2001; 3 days; Dose (3 mg/kg/day); Controls received mp w/ vehicle; animal info (polyarthritic male sprawg dawley rats, 6 weeks old); behavioral testing (foot withdrawal (pain)); Therapeutic indication (Rheumatoid arthritis);.


ALZET Comments: Diethyldithiocarbamate, Sodium;; PBS, sterile;; SC;; Rat;; 2ML2;; 7, 9 days;; controls received mp w/vehicle; functionality of mp verified by plasma levels; comparison of IP injections vs. mp; agent also called Ditiocarb or DDTC; arthritis;.


ALZET Comments: Interleukin-1 receptor;; Saline;; SC;; rabbit;; 14 days;; controls received mp w/vehicle; functionality of mp verified by plasma levels; immunology; peptides; arthritis; soluble interleukin-1 type II receptor used;.


ALZET Comments: Hoe 140; Bradykinin, Lys-Leu8-des-Arg9; Saline, sterile; SC; Rat; 1007D; 6 days; controls received mp w/ vehicle; peptides; agents administered singly and in combination.


ALZET Comments: Interleukin-10; PBS, sterile; SC; Rat; 2ML2; 14 days; controls received mp w/ PBS; comparison of footpad injections vs. mp; immunology; peptides.


ALZET Comments: Interleukin-1 receptor antagonist, recomb. human; IP; Mice; 1007D; 7 days; Controls received mp w/ BSA; immunology.

**ALZET Comments:** Interleukin-1 receptor antagonist; IP; mice; 1007D; no duration posted; controls received empty pumps or mp w/ vehicle; immunology.


**ALZET Comments:** Interleukin-1 receptor antagonist; IP; 7 days; brief mention of mp on p. 247; immunology.


**ALZET Comments:** Cyclosporin A; PEG 300; SC; Rat; 2ML4; no duration posted; photo of rat showing implanted pump (pg. 204); no stress (see pp. 199, 204, 205); immunology; controls received sham surgeries.


**ALZET Comments:** GI168; DMSO; Sodium citrate buffer; SC; Rat; 2ML2; 2 weeks; controls received mp w/vehicle; dose-response (see p. 451); immunology; multiple pumps per animal (2); "GI168 had poor oral bioavailability and a short plasma t 1/2 after subcutaneous injection... so minipump delivery was evaluated." p. 451; enzyme inhibitor (matrix metalloproteinase).


**ALZET Comments:** Morphine sulfate; Naloxone HCl; Saline; SC; Rat; 2ML4; no duration posted; controls received mp with saline or were naive.


**ALZET Comments:** Castanospermine; Mannose, D-; Phosphate, mannose-6-; Phosphate, fructose-1-; Saline; SC; IP; Rat; 2002; 14 days; controls received mp with saline or sham operation; comparison of drinking water admin. of CS vs. mp; immunology.


**ALZET Comments:** Nicotine hydrogen tartrate; ICI-118,551 Hexamethonium chloride; Saline; Ethanol; SC; Rat; 2ML2; 2ML4; 16,30 days; comparison of sc injections vs. mp; immunology; ICI-118,551 is a b2-adrenoceptor antagonist; antihypertensive.


**ALZET Comments:** Tumor necrosis factor-a; Albumin, bovine serum; Water; Rat; 2ML4; 28 days; peptides.


**ALZET Comments:** Interleukin-6; PBS; Serum, mouse; SC; mice; 2ML2; 2ML4; 2, 4 weeks; immunology; peptides.


**ALZET Comments:** Interleukin-2, PE40; NAD; IP; Rat; 2001; no duration posted; functionality of mp verified by serum levels of IL-2-PE40; comparison of of bid ip injections vs. mp; no stress (see pg. 314); stability achieved for 6 days by adding NAD (p. 308); multiple pumps per animal (2); half-life of 1-2 hours when given ip.
ALZET Comments: Cyclosporin A; PEG 300; Rat; 2ML4; 28 days; dose response (graph, p. 1284); immunology.

ALZET Comments: Interleukin-1; Collagenase, APMA-activated; Albumin; Saline; knee (articular cavity); rabbit; 2ML1; 7 days; stability verified in vitro for 7 days at 37 degrees C; collagenase was aminophenyl mercuric acetate-activated.

ALZET Comments: HETE, 15-; Saline; knee (articular cavity); dog; 2ML2; 2ML4; 10 days; tissue perfusion (knee joint).

ALZET Comments: Interleukin-1, alpha recomb. human; Interleukin-1, beta recomb. human; PBS; SC; mice; 2002; 7-14 days; dose-response; cancer/immunology; peptides.